MORPHOLOGICAL AND MICROCHEMICAL VARIATIONS IN MITOCHONDRIA IN THE NERVE CELLS OF THE CENTRAL NERVOUS SYSTEM

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TWO PLATES

One of the landmarks in neurology is the demonstration by Nissl in 1885 that different types of nerve cells may be distinguished from one another by the arrangement of the basophilic material within them. By common consent this basophilic material came to be called the Nissl substance. This departure in neurology, new at that time, proved extremely fruitful. Investigators flocked to the study of the Nissl substance and through their investigations brought to light many facts of fundamental importance. Since the arrangement of the Nissl substance is more or less specific in different types of cells it was thought that the cells might well be functionally as well as structurally different, just as muscle cells of different structure, gland cells and blood cells of different appearance are assumed to function differently. Thus arose the doctrine of neurone specificity according to which it is supposed that the nervous impulse varies in character with different cell types.

Through the recent discovery of mitochondria in the cells of the central nervous system it has become possible to attack this old problem from a new point of view and with greatly improved methods of technique. The object of this investigation is to ascertain whether the morphology and microchemical reactions of the mitochondria vary in different types of nerve cells. It is essentially a study of qualitative mitochondrial variation, and as such it is supplementary to the investigation of Thurlow ('16, p. 253) on quantitative variations. The Nissl substance as we see it in fixed and stained preparations is undoubtedly an artefact (Mott '15, p. 68, who unfortunately extends his artefact idea to the mitochondria also), caused by the action of the fixative upon a material present as a diffuse deposit in living cells, which fact does not, however, detract in any way from the value of the numerous detailed and careful observations on Nissl bodies in fixed tissues, because obviously, changes in the character of the coagulum (or precipitate) must be the visible manifestation of either quantitative or qualitative variations in the diffuse deposit occurring in the living cell. But it is important to note that the morphology of mitochondria in fixed preparations of nerve cells is, so far as can be ascertained, identical with that seen in the living condition, which of course gives additional value to observations on mitochondria. Then again mitochondria are bodies quite different chemically from the Nissl substance, playing in all probability an altogether different rôle in the cell economy.

It is clear then, that although this study of their morphology will be complementary and supplementary to the older work, it should enable us to push our investigations much further than is possible with studies upon the Nissl substance alone.

Comparatively little has been done thus far by other workers, who have, for the most part, confined themselves to determinations as to whether or not mitochondria do occur in adult nerve cells and to the relations of mitochondria to other constituents of nerve cells. The only paper on the mitochondria in the different kinds of nerve cells, apart from several preliminary notices of a page or more, is one by Busacca Archimede ('13, p. 322) on Testudo Graeca. No precise information has been gathered regarding qualitative variations in mitochondria in the nerve cells of the brain of any animals above the reptiles, or below them, for that matter. The following investigation was undertaken with the hope of being able to fill up this gap to a certain extent by careful study of a mammal.

MATERIAL AND METHODS

White mice of known age were used. Care was taken that they were in good condition. They were killed with chloroform, thus reducing the possible factor of fright to a minimum. They were then fixed by injection through the blood vessels of a mixture of formalin and bichromate so as to guard against the production of mechanical injury on removal of the brain as well as to insure a good penetration of the fixative. Sections were stained according to the method recommended by Cowdry ('16 b, p. 30), the essentials of which follow: (1) a fixation by injection, through the blood vessels, of a mixture of neutral formalin and potassium bichromate; (2) a mordanting in bichromate, followed by dehydration and imbedding in the usual manner; and (3) a staining of the sections, cut 4 microns in thickness, with fuchsin and methyl green. The fuchsin stains the mitochondria a bright crimson color and the methyl green colors the Nissl substance in the same cell green, thus giving a good color contrast between the two. Specimens were also stained with iron hematoxylin and by the Benda method, for control. They gave results confirmatory in every way.

The observations are based upon actual measurements of mitochondria which were made by using one of the new Spencer wheel ocular micrometers. Each measurement was made five times and the average taken so as to reduce the experimental error as far as possible.

OBSERVATIONS

Morphological variations. A general survey of the central nervous system was made and it became at once evident that the mitochondria did present considerable variation in form in different types of nerve cells. Nerve cells of the same kind, in the same nuclei, generally contained the same form of mitochondria. Somewhat more individual variation appeared in cells of the spinal cord, spinal ganglion and Gasserian ganglion, due perhaps to mechanical injury on removal. Mechanical manipulation and faulty technique will bring about great variation in the morphology of mitochondria occurring in the same type of cells, in a single center, which actually possess similar mitochondria. In fact one comes to suspect those preparations which exhibit a great dimorphism of mitochondria in cells of the same type. Poor penetration of the fixative generally results in the filamentous mitochondria breaking up into granules, or else forming spherules; a phenomenon well known in other tissues. There is no evidence that filaments are ever formed as a result of bad technique. In all my observations a careful check has been kept upon the technique.

In some nerve cells, like the anterior horn cells of the spinal cord (fig. 1), and the large cells of the reticular formation of the midbrain (fig. 11), the mitochondria are present in the form of filaments of variable length, which frequently attain a length of 4.66 microns in the former and 6.49 microns in the latter. They are much longer in the processes than they are in the cell body. They are more granular in the immediate vicinity of the nucleus where they are also more numerous. This is a striking feature of all the cells observed. It is well to remember at this point that filamentous mitochondria occur in other types of cells also; indeed, filamentous mitochondria occur more frequently than any other form in the central nervous system.

Again we find cells with mitochondria in the form of granules or short plump rods. The cells of the mesencephalic nucleus of the trigeminal nerve (fig. 5) are crowded with mitochondria of this description. The granules are about 0.29 microns in diameter and the filaments about 0.62 microns long. Mitochondria of intermediate size and shape are invariably to be seen. It is interesting to note that the same sort of mitochondria are encountered in the large cells of the Gasserian ganglion, because the nature of these mesencephalic cells has been long in dispute and this new point of similarity between them and cells known to be sensory constitutes additional evidence that they themselves are sensory, and as Thurlow[1] also has emphasized, supports the view that they are in reality neural crest cells which have been enclosed in the neural tube in the course of development. This

[1] Thurlow, personal communication.

similarity is the more striking when we bear in mind that granular mitochondria are not at all common in the cells of the central nervous system. The small cells of the Gasserian ganglion contain exceedingly minute granular mitochondria (fig. 6) which are usually clumped together in the vicinity of the nucleus leaving the peripheral cytoplasm free. This last fact considered in connection with Cowdry's ('14, p. 27, fig. 13) demonstration of mitochondria of like nature and distributed in the small cells of the spinal ganglion, which Ranson ('14, p. 123) believes to be concerned in conduction of pain and temperature sensations, is significant. One might expect similar functions to be the property of these cells, and we should be on the lookout for changes in them in cases of trifacial neuralgia.

All nerve cells, even those with otherwise granular mitochondria invariably contain filamentous mitochondria in their processes, whether they be dendrites or axones, from which it follows that there is greater variation in the mitochondria in cell bodies than in cell processes. It may be recalled that the mitochondria are all filamentous in the cells of the neural tube of the developing embryo. In other words, mitochondria retain their embryonic form in the processes and become specialized in the cell bodies. The mitochondria are usually filamentous in the axone hillock.

The cells of the nucleus of the corpus trapezoideum present as peculiar a picture as is found in any other part of the nervous system (fig. 2). Large block-like mitochondria are found in the peripheral layer of the cytoplasm. The large mitochondria are frequently oblong. Some of those illustrated in the figure are as much as 1.74 microns long by 0.63 microns in breadth. This suggests a possible relation to the unique synaptic connection of these cells (Collin '05, p. 313). The peculiarity of the connection lies in the very large pericellular fibres which arborize about the cell circumference and encompass it in a sort of cone. Nowhere else in the nervous system do we find such large fibres making connections of this kind. Further examination of the cell shows, more centrally, a distinct diminution in the size of the mitochondria which here occur as small grains or filaments, almost beyond the limits of accurate measurement. Comparatively large areas of cytoplasm seem to be devoid of mitochondria. An abrupt change occurs in the form of mitochondria as we pass to the neighboring cells of the pontile nucleus, in which the block-like mitochondria, as well as the peculiar synapses, are absent.

It has been generally assumed (Busacca Archimede '13) that the mitochondria occur between the Nissl bodies and not within them. So far as I have been able to ascertain, with a method of staining which permits of observation of Nissl substance and mitochondria at the same time, this is not the case. Indeed one would not expect to find the mitochondria between the Nissl bodies in view of the fact which Cowdry ('14, p. 20) emphasizes, that the Nissl substance is present as a homogeneous diffuse deposit in the living cell and that the Nissl bodies as seen in the fixed preparations are produced by a process of coagulation or precipitation.

It may be mentioned in passing that cells with the typically filamentous variety of mitochondria (reticular formation cells, fig. 11), the granular or rod-like mitochondria (mesencephalic cells, fig. 5) and the blocklike mitochondria (cells of trapezoid nucleus, fig. 2) all occur in the same section, proving that the differences in form of mitochondria cannot be due to variations in technique. Furthermore the variations in morphology were found to occur constantly in all members of the species which were examined.

Another fact worthy of note is that cells of quite different type like the mitral cells of the olfactory bulb (fig. 3), the Purkinje cells of the cerebellum (fig. 9), and the cells of the septum (fig. 10) all contain mitochondria of the same kind. It is clear that variations in the form of mitochondria cannot be used to differentiate between sensory and motor cells, nor can quantitative variations be so used, according to Thurlow ('16, p. 253). This is in marked contrast to variations in the Nissl substance, which can be used for such differentiation (Malone '13, p. 129). Again, the general assumption that the morphology of the mitochondria is related to the shape of the cell containing them does not seem to hold, for instance, the shape of the cells of the corpus trapezoideum (fig. 2) and the cells of the corpus striatum (fig. 8) is somewhat similar, yet the mitochondria in them are quite different. An inspection of the cells of the mesencephalic nucleus of the trigeminal nerve (fig. 5) and of the large and small cells of the Gasserian ganglion (figs. 6 and 7) shows that the mitochondria are rod-like or granular when present in great abundance (which would agree well with Dubreuil's hypothesis to be mentioned subsequently). I have not observed any change in the nucleus, or in the nucleoli, or in the Nissl substance, or indeed in any other cell structure which runs parallel with the above mentioned variations in mitochondria and which might offer a possible explanation of them. I have observed mitochondria in the surrounding cell processes but am unwilling to state that they actually occur between the cells themselves (that they are intercellular).

I have not found mitochondria with the bleb-like swellings, which are so common in secreting cells; or in networks. (All the net-like formations observed are illusory, being due to superposition of individual filaments, which can usually be resolved by careful focussing.) Neither have I seen them swell up to form vacuoles with clear centers, and there is no evidence of an agglutination of mitochondria as occurs in pathological conditions (Scott '16, p. 249). I should therefore feel that the occurrence of such mitochondria was evidence of pathological change.

Microchemical variations. In the inspection of a large amount of material a certain number of brains were studied, which were for some reason poorly fixed, and it was noted that in these, certain groups of cells contained mitochondria while others did not. An instance in point is that of a brain in which it was observed that, while all the cells of the mesencephalic nucleus of the trigeminal nerve contained their normal complement of mitochondria, the neighboring cells of the locus cœruleus, scattered among them were found to be devoid of mitochondria. In order to ascertain whether there were differences in the solubility of mitochondria beyond chance variations, the following experiment was carried out.

Brains of mice were fixed by injection in the regular manner, with the formalin bichromate mixture to which in one case 0.5 per cent, in another 1 per cent, in a third 2.5 per cent, in a fourth 5 per cent and finally 10 per cent of acetic acid had been added. They were carried through and stained in the usual way.

No mitochondria were found after using the mixture containing 10 per cent acetic acid except in the cells of the hypophysis. This was also true in the case of the 5 per cent mixture. With increase in concentration of acetic acid the sections became more and more difficult to stain and required longer and longer treatment with permanganate and oxalic. The fluid containing 2.5 per cent acetic acid gave apparently the same fixation as the 5 per cent mixture, but the 1 per cent acetic mixture preserved the mitochondria in the Purkinje cells of the cerebellum and destroyed the mitochondria in the nerve cells of the medulla.

With regard to variations in staining reactions it need only be said that we do observe mitochondria taking the stain more intensely in certain parts of the cell. This is often the case in the region of the axon hillock. As the staining reaction does not occur regularly and inasmuch as it may be due to differences in the degree of mordanting with the bichromate I am not inclined to attach much significance to it. Moreover when mitochondria are very abundant they sometimes stain more intensely, which may be due to the presence of the stain in greater mass and consequently washing out more slowly than where only a few mitochondria occur. Careful search has not revealed any definite difference in the staining reactions of the different forms of mitochondria, although one might expect this, if differences in morphology were assumed to be related to differences in density.

DISCUSSION

Significance of morphological variations in mitochondria. The true significance of the morphological variations in mitochondria is unknown. Yet the demand for information is very insistent as it is highly desirable that we should in some measure understand the variations which unquestionably do occur both in normal states and in pathological conditions. Two important interpretations have been advanced.

Rubaschkin ('10, p. 428) found, in the study of guinea pig embryos, that the mitochondria were granular in the primordial germ cells and filamentous in other more specialized epithelial cells. He arrived at the general conclusion that the primitive granular form of mitochondria is peculiar to undifferentiated cells and that the process of differentiation shows itself by a change of the primitive granular type into chain-like and filamentous forms. This view has been much criticised. It is inconsistent with the investigations of Swift ('14, p. 495) who found that in the primordial germ cells of the chick the mitochondria are rodlike and do not differ from those in somatic cells. It is sufficient merely to state that my observations, that granular mitochondria occur constantly in some types of nerve cells and filamentous ones in others, are also at variance with Rubaschkin's hypothesis, because both the types of nerve cells in question (large cells of the Gasserian ganglion (fig. 7) and anterior horn cells (fig. 1)), are undoubtedly highly differentiated.

Dubreuil ('13, p. 137), on the other hand, is of the opinion that granular mitochondria are in a state of rapid multiplication by division and are characteristic of active stages in the life of the cell and that filamentous ones are indicative of rest. He bases this belief upon his study of the changes which the mitochondria undergo in the development of fat cells from fixed connective tissue cells. He found that when the cells are most active the mitochondria are most numerous and are granular; when the cells are less active the mitochondria are filamentous and less abundant. He adds to this the observation that when inflammation sets up, the mitochondria immediately increase greatly in number and are granular. The observations recorded in this paper would, at first sight, seem to support this view, for an inspection of the plates reveals at once that where the mitochondria are most abundant, that is to say in cells of the mesencephalic nucleus of the fifth nerve (fig. 5) and in the large cells of the Gasserian ganglion (fig. 7) they are also granular. The contention is, however, ruled out, by the fact that in other tissues the mitochondria may still be filamentous even though they be increased greatly in amount (Policard, '10, p. 284).

The variations in the form of mitochondria must be due to differences in themselves or in their environment or in both.

There is evidence that the chemical constitution of mitochondria is different in different cells. Regaud ('10, p. 301) has shown that there is a progressive increase in the resistance of mitochondria to acetic acid in the course of spermatogenesis. My experiments have shown that the mitochondria in the nervous system also differ in their susceptibility to acetic acid. In the nervous system this difference in chemical behavior does not seem to be related to a difference in morphology, as mitochondria of quite different form exhibit similar solubilities. So much for chemical composition. Now with regard to density, the only indicator which I have is the difference of intensity in staining with fuchsin and as I have said this is not uniform and is of uncertain meaning. That the form of mitochondria is, in a measure dependent upon their own organization is evident when we remember that if the long filamentous mitochondria in the acinus cells of the pancreas are squeezed out of the cell into the surrounding fluid they maintain their original form, unaltered, for a surprisingly long time.

As to the differences in the cytoplasm in which the mitochondria are embedded I have observed that the cells of the mesencephalic nucleus of the trigeminal nerve are more noticeably shrunken in some preparations than the other cells in the vicinity, which may be accounted for on the assumption of a higher water content. The difference in form of mitochondria and of water content of their surroundings may not be unrelated. As has been noted the mitochondria are invariably filamentous in the processes, though they may sometimes be granular in the cell bodies. This led to the belief, that there might be a difference in water content in gray and white substance of the brain, which curiously enough, was found, on looking up the literature, to be actually the case. The possible influence of the water content seems the more likely since Löwschin ('13, p. 203) has been able to alter the form of his artificial mitochondria, made out of lecithin, by varying the physico-chemical properties of their environment. Since there is a general concensus of opinion in favor of the view that mitochondria are a combination of lipoid and albumin it is possible that alkalinity or acidity would affect their form. The acidity acting upon the protein fraction might cause it to become hygroscopic and to swell (Cowdry '16b, p. 440). The fact that the Nissl bodies, as well as the mitochondria, are often larger in the peripheral cytoplasm than they are in the immediate vicinity of the nucleus, would seem to indicate that some common environmental factor may be operating in the case of both, notwithstanding the fact that the Nissl bodies are probably a coagulum or a precipitate resulting from fixation.

In a general discussion of this kind the mechanical factors which sometimes operate, in the surrounding fluid, in shaping the morphology of mitochondria must not be lost sight of. Thus N. H. Cowdry has observed the changes in the form of mitochondria in the streaming protoplasm of living plant cells. He has seen straight filaments assume the form of loops and spirals in response to currents and eddies in the stream, indicating clearly that they are flexible and that their form is in a measure determined by their environment. Conditions of protoplasmic stress and strain, occurring especially in the course of development, probably influence the form of mitochondria also. In the outgrowing nerve fibers, for instance, the mitochondria are generally filamentous. Whether mechanical factors of this sort may play any considerable rôle in determining the form of mitochondria in adult nerve cells is unknown. It is highly probable that some combination of the two factors of variation in internal composition and of changes in the surroundings are mutually responsible for the variations in form observed.

Bearing upon doctrine of neurone specificity. These observations on variations in the morphology of mitochondria bring to light another specific difference between the internal structure of nerve cells of different categories; for it has already been pointed out that these differences in the form of mitochondria are in all likelihood associated, in some obscure way, with changes in their environment; that is, in the cytoplasm. The intimate bearing of such differences in the cytoplasm upon the doctrine of neurone specificity is apparent, inasmuch as any difference in the specialized activity of a cell, like conduction, is in all probability related to some difference in the cytoplasm rather than in the nucleus. This is not at variance with the results which others have obtained.

Since Cowdry ('14, p. 21) has found that there is a surprising constancy in the mitochondria in the spinal ganglion cells of different vertebrates, including man, it is altogether likely that the variations in morphology which I have described in the mitochondria in different types of cells in the brain of the white mouse may hold in other mammals also. This seems to indicate that when differences in the morphology of the mitochondria occur they are not chance variations but are fundamental differences ingrained in the very organization of the cell.

Moreover Thurlow ('16, p. 253) has found, by a detailed quantitative study of mitochondria in the cells of the different cranial nerves, that the actual number of mitochondria per unit volume of cytoplasm varies considerably. The largest amount of mitochondria was found by her in the cells of the mesencephalic nucleus of the trigeminal nerve and the least in the visceral motor nucleus of the seventh. Even if we adopt the ultraconservative view that the mitochondria are purely deutoplastic elements and do not play an active rôle in cellular physiology (which I would be loath to do) it is perfectly obvious that their presence in great amount in some cells and in very small numbers in others, must indicate either a qualitative or else merely a quantitative difference in the nature of the activity of the cells in question. For it is impossible to regard the activity of a cell as being entirely uninfluenced by the heaping up in it of inert substances.

Pathological bearing. The practical value of this work lies in its possible pathological application. The standardization of material for experiment, the enumeration of the qualitative variations which normally occur in mitochondria in the different types of nerve cells of the central nervous system of a mammal and the mention of the forms of mitochondria which should, in any experimental study of the nervous system, be regarded as pathognomonic (i.e., net-works, bleb-like swellings, agglutinations and vacuolations), are all of interest from a pathological point of view. The necessity of taking cognizance of mitochondrial changes is brought home to the clinician through the recent investigations of Goetsch ('16, p. 132) who found that an increase in the mitochondria in the thyroid epithelium was associated with an increase in the activity of the epithelial cells and with the severity of the clinical symptoms of hyperthyroidism in man.

As nothing has yet been done on the changes in the mitochondria in the nerve cells of man in pathological conditions it is quite clear that the following are merely suggestions.

If Regaud ('11, p. 20) is at all justified in his statement that "by a still unknown physico-chemical mechanism, the mitochondria retain a great variety of substances which come in contact with the protoplasm, normally as well as accidentally (medicines, poisons, toxins, etc.)" and if the conclusion is warranted that the point of action of tetanus toxin on the nerve cell is lipoidal, it is quite possible that a study of mitochondria in the nervous system in tetanus might yield interesting results. At any rate the fact that tetanus toxin is rendered innocuous when mixed with an emulsion of brain pulp (Wassermann and Takaki '98) is evidence that the toxin combines with some component of nerve tissue. Leathes ('10, p. 123) believes that it acts upon a fat which he calls 'cerebrone.'

There are up to the present no observations on mitochondria in nerve regeneration, although there is evidence from many sources that the mitochondria are delicate indicators of cell activity, and may reveal interesting facts with regard to the formation of myelin, etc.

Pathologists have frequently noted that the mitochondria are the first structures in the cell to respond to disturbances in function, which suggests the possibility that a study of them in the nervous system may serve to localize brain lesions which heretofore have eluded the grasp of neurologists. One would naturally inquire first into those diseases in which chemical analysis has revealed a disturbance in the lipoid content, particularly general paralysis since Koch and Mann ('09) have detected a destruction of the brain phosphatides in this condition and there is a good deal of evidence that the mitochondria are, themselves, closely related to phosphatides.

Before concluding I want to express my deep appreciation to Dr. E. V. Cowdry for his friendly interest and encouragement.

SUMMARY

There are qualitative differences in the mitochondrial content of certain types of nerve cells in the brains of white mice. The variation in morphology between cells of different variety is often quite pronounced. Filamentous mitochondria are the most common form met with in the cells of the central nervous system. They are particularly apparent in large anterior horn cells (fig. 1) and in the large cells of the reticular formation (fig. 11). Rod-like and granular mitochondria are rarer. They are characteristic, however, of the cells of the mesencephalic nucleus of the fifth nerve (fig. 5) as well as of the cells of the Gasserian ganglion (figs. 6 and 7). The cells of the nucleus of the corpus trapezoideum (fig. 2) may be distinguished by their large, swollen block-like mitochondria.

There is also, in the majority of cases, a variation in the form of mitochondria in different parts of the same cell. For instance, they are usually more granular in the vicinity of the nucleus than in the peripheral parts of the cytoplasm, and in the processes. In the processes they are invariably rod-like or filamentous. This is shown in most of the drawings but it is particularly well illustrated in figures 1, 5, 9, 10, 11 and 12. The cells of the nucleus of the trapezoid body constitute a special case because in them the mitochondria always occur in the form of long blocks in the peripheral cytoplasm in sharp contrast to the minute granular and rod-like mitochondria in the immediate neighborhood of the nucleus. The mitochondria occur not

only between the Nissl bodies (as is generally believed) but also embedded in them.

They also vary in different kinds of nerve cells microchemically. The most striking instance is the greater resistance of the mitochondria in some cells to fluids containing acetic acid as compared with other cells of different types. The mitochondria in the different parts of the cytoplasm of the same cell react in the same manner to solvents.

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DESCRIPTION OF PLATES

The figures have been drawn from cells in the central nervous system of a female white mouse, thirty-five days old, weighing 9 grams, body length 6.8 cm. and tail length 6.1 cm., fixed in neutral formalin and bichromate and stained with fuchsin and methyl green. By this method the mitochondria are stained bright crimson against a green background of Nissl substance. The mitochondria are represented in black in the illustrations which were drawn with Zeiss apochromatic objective 1.5 mm., compensating ocular 6 and camera lucida. The figures are reproduced without reduction so that they represent an actual magnification of 1660 diameters as they now appear on the plates. They are intended to illustrate differences in the morphology and in the arrangement of mitochondria, which are peculiar to and which are constantly met with, in certain types of nerve cells in the brains of white mice.

PLATE 1

EXPLANATION OF FIGURES

1 Large anterior horn cell of the spinal cord in which the mitochondria are typically filamentous. They are longer in the processes than they are in the neighborhood of the nucleus. They may be seen imbedded in the flake-like Nissl substance.

2 Cells from the nucleus of the corpus trapezoideum. The striking feature is the presence of relatively enormous block-like mitochondria in the peripheral cytoplasm, leaving certain areas devoid of mitochondria. It is to be noted furthermore that the mitochondria are quite minute in the immediate vicinity of the nucleus. A large pericellular arborization is visible between the two cells.

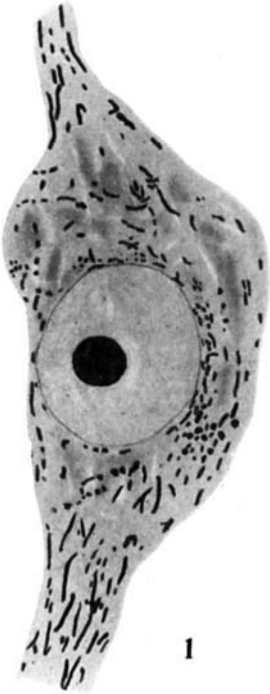
3 A mitral cell from the olfactory bulb. Filamentous mitochondria are to be seen embedded in a homogeneous background of Nissl substance.

4 Large pyramidal cell from the hippocampus showing practically the same arrangement of mitochondria as in the preceding.

5 A large cell of the mesencephalic nucleus of the fifth nerve with a cell of the locus cœruleus immediately adjacent. This large cell is among the most remarkable seen in the whole nervous system. It contains large numbers of small rod-like mitochondria and the striking resemblance which it bears to the large cells of the Gasserian ganglion (fig. 7) is at once apparent.

6 Small cell of Gasserian ganglion with minute granular mitochondria clumped about the nucleus.

7 Large cell of Gasserian ganglion containing an abundance of granular mitochondria in sharp contrast with the filamentous mitochondria which occur in the majority of other nerve cells.



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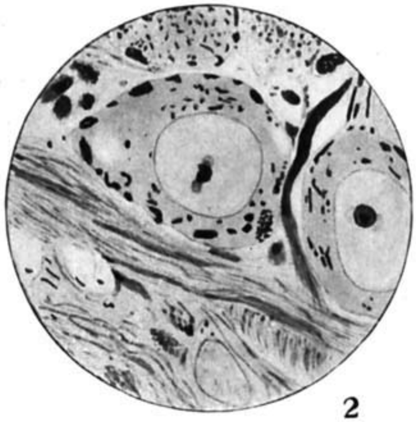

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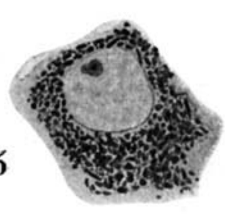

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PLATE 2

EXPLANATION OF FIGURES

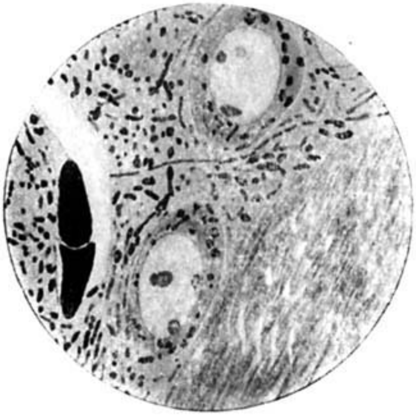
8 Two cells of the corpus striatum. They contain spherical and rod-shaped mitochondria which, in fact, resemble closely the fine medullated fibres cut in section in the neurophil about them. To the left two red blood cells are to be seen in a capillary.

9 Large pyramidal cell of the cortex cerebri with its contained mitochondria which are quite filamentous. This cell also is embedded in a mass of fibers which are cut in section and which resemble mitochondria very closely.

10 A cell from the septum.

11 Large cell from the formatio reticularis of the mid brain. The mitochondria are thread-like and remind one of those which occur constantly in anterior horn cells. They are, as is invariably the case in all the cells studied, more filamentous in the processes than in the cell body.

12 Purkinje cell of the cerebellum with neighboring granule cells just beneath it. The mitochondria look like minute bacilli near the nucleus but they become elongated as one proceeds toward the great dendrite. The granule cells also contain them. The black dots in the molecular layer are cross sections of fibres.



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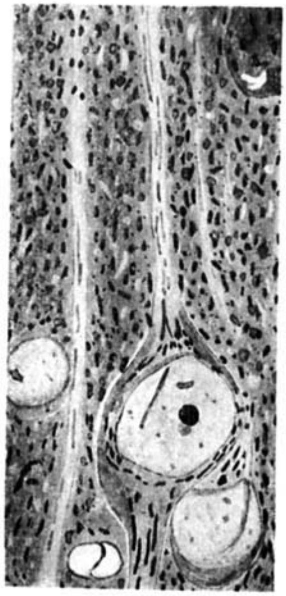

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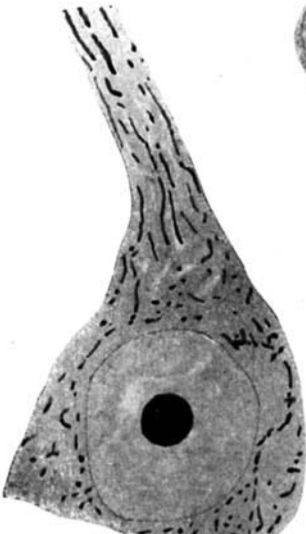

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